Remarks/Arguments

Prior to the present amendments, claims 1-7 were pending in this application and were rejected on various grounds. Claims 1 and 7 have been amended and new claims 8 and 9 have been added. The amendments and new claims are fully supported by the specification and do not add new matter. Specific support for the amendments and new claims is at least at page 6, 15-20 and page 18, lines 18-21.

All amendments were made without prejudice or disclaimer. Applicants explicitly reserve the right to pursue any deleted subject matter in one or more continuing applications.

The current amendments do not require new, extensive search or consideration by the Examiner, and are believed to place the application in *prima facie* conditions for allowance, or, at least, present the claims in better form for consideration on appeal. Accordingly, the entry and consideration of the present amendments after final rejection is respectfully requested.

Claim Rejections – 35 U.S.C. § 103

Claims 1-7 were rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Sandbaek et al..... (Blood Coagulation and Fibrinolysis, 1999) as supported by DrugBank (def "Tenecteplase") in view of Graney et al. (Australian Patent AU-B-42810).

According to the rejection, "Sandbaek et al. teach a concentration of Alteplase in saline at a final concentration of 0.02 mg/mL" and its administration by an indwelling catheter (page 88, col. 1). According to the rejection, Alteplase is an art recognized equivalent for the same purpose as Tenecteplase. Although Sandbaek et al. does not teach the concentration recited in claim 5, citing M.P.E.P. § 2144.05 II, the Examiner asserts that generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art "unless there is evidence indicating that such concentration or temperature is critical." (Office Action, page 6)

Graney et al. was cited as allegedly teaching that Tenectaplase can be included in compositions where the solvent carrier is sterile water (page 7, line 8) or distilled water, Ringer's

solution as well as saline and other conventional carriers (page 8, lines 19 and 20). Again asserting that Tenecteplase and Alteplase are art recognized equivalents, the examiner concludes that "it would be obvious for one of ordinary skill in the art to substitute saline from sterile water for injection." (Office Action, page 6, last sentence)

Applicant's arguments in response to an earlier rejection under 35 U.S.C. 103 of claims 1-7 over Sandbeak et al. in view of Graney with support from DrugBank were not found persuasive, essentially for the following reasons:

(1) Although Alteplase and Tenecteplase are not identical, in view of their "close structural similarity and catalytic activity towards the dissolution of thrombi," absent evidence to the contrary, one would expect the similar results for Alteplase as that for Tenecteplase (Office Action, passage bridging pages 2 and 3).

(2) Absent any evidence of criticality of the effect of their concentrations in solution on the catalytic reaction performed by these enzymes, "it remains obvious to use the same concentration of Tenecteplase as you would for Alteplase" (Office Action, page 3, first full paragraph).

(3) The argument that the invention is useful for treating pathological collection of fibrin-rich fluid in catheter, to provide catheter cleansing "is not commensurate to the scope of the claims which are to a composition and not a method." Citing M.P.E.P. 2111.02 II, the Examiner notes that "limitations implied in the intended use are considered only if they impart a structural limitation." (Office Action, page 3, second full paragraph)

(4) In addressing Applicant's argument that the solution of Sandbaek et al. is not allowed to dwell in the catheter, the Examiner notes that the term "dwell" is not defined in the specification, and therefore, it is interpreted to mean "to remain for a time." Using this definition, the Examiner concludes that in Sandbaek et al. the Alteplase solution does remain for a time in the catheter, and thus "dwells" within the catheter.

(5) The fact that Graney does not teach the use of Alteplase for a clearing out a catheter was not considered relevant, since the claims are directed to a composition and not to a method.

Applicants disagree and respectfully traverse the rejection.

Claim 1 has been amended to recite that the tenecteplase solution of the invention is comprised within an indwelling catheter in which the flow of the fluids is obstructed by fibrin-bound blood clots, for a least about 5 days. This amendment should obviate reasons (3)-(5) above for finding Applicant's earlier arguments not persuasive. Since the claim now specifically recites that the solution is in an indwelling catheter, the difference between Sandbaek et al, which describes a well-known method of using native-sequence t-PA (alteplase) to dissolve blood clouts in native arteries and grafts, and the present invention, which concerns the non-toxic removal of fibrin-bound blood clots from an indwelling catheter, is clearly reflected by the language of claim 1. Similarly, since the claim now recites that the tenecteplase solution is present in the catheter for at least about 5 days, the Examiner's findings based on the ordinary meaning of "dwell" no longer apply. As explained in Applicant's earlier response, in Sandbaek et al. the alteplase solution is not allowed to stay in the catheter for any extended period of time, let alone 5 days, since the catheter simply serves as a conduit to deliver the drug to the clot.

As far as the alleged equivalence of alteplase and tenecteplase is concerned, Applicants submit that the two plasminogen activators are not equivalent for the use recited in the claims of the present application. Due to its lower potency, alteplase would be unexpected to effectively remove fibrin bound clots from an indwelling catheter in the concentration rages and within the time period recited in the claims. Furthermore, from the teaching of Sandbaek et al. of using alteplase in a dynamic therapeutic setting, one of ordinary skill in the art would not be able to extrapolate the concentration range and the dwell time which are required to ensure that tenecteplase, a significantly different plasminogen activator, effectively remove fibrin-bound blood clots from an indwelling catheter,

Since Graney does not compensate for the deficiencies of Sandbaek et al., the cited combination of references does not make obvious the invention claimed in the present application, and the present rejection should be withdrawn.

Claim Rejections – 35 U.S.C. § 112

Claim 7 has been rejected under 35 U.S.C. 112, second paragraph as allegedly being indefinite in its recitation of "An indwelling catheter with no occlusions wherein."

Claim 7 has also been rejected under 35 U.S.C. 112, first paragraph for its recitation of the same phrase, for which no support was found in the specification.

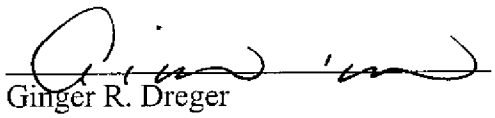
Since the phrase objected to is no longer present in claim 7, these rejections are believed to be moot.

All claims pending in this application are believed to be in prima facie condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, or credit overpayment to Deposit Account No. **08-1641** (referencing Attorney's Docket No. **39766-0239R1**).

Respectfully submitted,

Date: January 18, 2008



Ginger R. Dreger
Reg. No. 33,055

HELLER EHRMAN, LLP
Customer No. 25213
275 Middlefield Road
Menlo Park, California 94025
Telephone: (650) 324-7000
Facsimile: (650) 324-0638

SV 2327598 v1
1/17/08 1:00 PM (39766.0239)